cancer [cell] cellular morphology in all [nucleated] epithelial cancer cells in the blood sample;

d) placing the blood sample in the [tube] container and centrifuging the blood sample in the [tube] container so as to cause [any differentiated pathologically abnormal nucleated] epithelial cancer cells present in the blood sample to [gravitate by density into] localize in said [well-defined zone] free volume in the [tube] container;

e) enumerating any differentiated [pathologically abnormal] epithelial cancer cells found in situ in the [well-defined zone] free volume in the [tube] container;

f) examining the [cell] morphology of any differentiated [pathologically abnormal] epithelial cancer cells in situ in the [well-defined zone] free volume in the [tube] container;

g) said combining steps being performed either before or after the blood sample is placed in the [tube] container; and

h) said enumerating and examining steps being performed in no particular order.

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2.(amended) A method for detecting the presence or absence of cancerous cell morphology in circulating [target pathologically abnormal nucleated] epithelial cells in a centrifuged sample of anticoagulated whole blood contained in a [tube] container which [tube] container also contains [a generally cylindrical] an insert which forms a [well-defined annular zone] free volume in the [tube] container, said blood sample having been combined with one or more labeling agents that are specific to one or more epitopes on the [pathologically abnormal target nucleated] epithelial cells, and said blood sample having also been combined with a colorant which is operable to clarify epithelial [cell] cellular morphology in [all nucleated] epithelial cells in the blood sample, said method comprising the steps of identifying [a percentage of all] labeled epithelial cells which are disposed in said [well-defined annular zone] free volume in situ in the [tube] container, and examining the cell morphology of any such identified epithelial cells in situ in the [tube] container so as to determine whether any such identified epithelial cells display [pathologically abnormal] cancerous cell morphology.

3.(amended) A method for [enumerating] identifying circulating cancerous epithelial cells in a centrifuged sample of anticoagulated whole blood which sample is contained in [a] an at least partially transparent [tube] container, which [tube] container

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also contains [a generally cylindrical] an insert, and which blood sample has been combined with at least one labeling agent that is specific to at least one epithelial cell epitope, and which blood sample has also been combined with a colorant that clarifies nucleated [cell] cellular morphology, said method comprising the steps of examining a [well- defined zone] free volume located between the insert and the [tube] container wall wherein [platelets] buffy coat constituents in the blood sample gravitate during centrifugation and [enumerating] identifying any labeled epithelial cells having [pathologically abnormal] cancerous morphology in situ in the [tube] container, which epithelial cells have localized during centrifugation in said [well-defined zone] free volume in the [tube] container.

B2 4.(amended) A method for differentiating cancer cells from hematologic progenitor cells and from other nucleated cells in a sample of anticoagulated whole blood, said method comprising the steps of:

a) providing a sample of anticoagulated whole blood containing epitopic cell labeling materials which are operable to differentiate cancer cells and hematologic progenitor cells from each other and from other nucleated cells in the sample, said sample being contained in [a] an at least partially transparent [tube] container which also contains an insert that is operable to form a well-defined [zone] free volume in the [tube] container;

b) centrifuging the sample of blood in the [tube] container so as to gravimetrically separate the blood sample into its formed cellular and platelet constituent components and so as to [settle by density] cause any nucleated cells which are not conventional blood cells in the sample to localize in said well-defined [zone] free volume in the [tube] container; and

c) examining said well-defined [zone] free volume in the [tube] container in order to determine whether any [differentiated nucleated] cancer and/or hematologic progenitor cells are present in said well-defined [zone] free volume in the [tube] container.

B3 5.(amended) A method for [enumerating] detecting cancer cells and/or hematologic progenitor cells in a sample of anticoagulated whole blood, said method comprising the steps of:

a) providing a sample of anticoagulated whole blood containing [epitopic] cell epitope

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labeling materials which are operable to differentiate cancer cells [and] and/or hematologic progenitor cells [from each other and] from other nucleated cells in the sample, said sample being contained in [a] an at least partially transparent [tube] container which also contains an insert that is operable to form a well-defined [zone] free volume in the [tube] container;
b) centrifuging the sample of blood in the [tube] container so as to gravimetrically separate the blood sample into its constituent formed cellular and platelet components and so as to [settle] localize any nucleated cells in the sample in said well-defined [zone] free volume in the [tube by density] container;
c) examining said well-defined [zone] free volume in the [tube] container in order to determine whether any epitopically differentiated nucleated cells are present in said well-defined [zone] free volume in the [tube] container; and
d) enumerating any cancer cells and/or hematologic progenitor cells which are found to be present in said well-defined [zone] free volume in the [tube] container.

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6.(amended) A method for analyzing a sample of anticoagulated whole blood in order to determine the presence or absence of cancer cells [and/or hematologic progenitor cells] in the sample, said method comprising the steps of:
a) providing a sample of anticoagulated whole blood containing [epitopic] cell epitope-labeling materials which are operable to differentiate cancer cells [and hematologic progenitor cells from each other and] from other nucleated cells in the sample [and containing a cell morphology-clarifying stain], said sample being contained in [a] an at least partially transparent [tube] container which also contains an insert that is operable to form a well-defined [zone] free volume in the [tube] container;
b) centrifuging the sample of blood in the [tube] container so as to gravimetrically separate the blood sample into its constituent formed cellular and platelet components and so as to deposit [by density] any [nucleated] cancer cells in the sample[, which are not blood cells], in said well-defined [zone] free volume in the [tube] container; and
c) examining said well-defined [zone] free volume in the [tube] container in order to determine whether any differentiated [nucleated] cancer cells are present in said well-defined [zone] free volume in the [tube] container.

7.(amended) A method of identifying circulating epithelial cancer cells in a centrifuged

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sample of anticoagulated whole blood which sample is contained in [a] an at least partially transparent [tube] container, which [tube] container also contains an [axially elongated] insert that forms a well defined [zone] free volume in the [tube] container, and which blood sample has been combined with at least one labeling agent that is specific to at least one epithelial cancer cell epitope, said method comprising the steps of examining said well-defined [zone] free volume in the [tube] container wherein white cells and platelets in the blood sample have gravitated during centrifugation and identifying any labeled epithelial cancer cells in situ in the [tube] container which labeled cells have localized in said well-defined [zone] free volume in the [tube] container during centrifugation of the sample in the [tube] container.

9.(amended) A method for detecting the presence or absence of circulating [target pathologically abnormal] nucleated epithelial cells in an anticoagulated whole blood sample, said method comprising the steps of:

a) providing [a] an at least partially transparent [tube] container having a bore containing an [axially elongated] insert, said [tube] container and insert combining to form a well-defined [zone] free volume in the container bore [tube];

b) combining the blood sample with one or more epitope-specific labeling agents so as to differentially highlight any [pathologically abnormal target] nucleated epithelial cells which may be present in the blood sample;

c) combining the blood sample with a colorant which is operable to clarify [cell] cellular morphology in all nucleated cells in the blood sample;

d) placing the blood sample in the [tube] container and centrifuging the blood sample in the [tube] container so as to cause any [pathologically abnormal] nucleated epithelial cells present in the blood sample to gather in said well-defined [zone] free volume in the container bore [tube];

e) enumerating any labeled epithelial cells found in situ in the well-defined [zone] free volume in the container bore [tube];

f) examining the cell morphology of any labeled cells in situ in the well-defined [zone] free volume in the [tube] container;

g) said combining steps being performed either before or after the blood sample is placed in the [tube] container; and

h) said enumerating and examining steps being performed in no particular order.

9 ~~10~~.(amended) The method of Claim 8 wherein said enumerating and examining steps are performed with [a] an automated [microscopical] microscope-like instrument.

~~11~~ 10 ~~11~~.(amended) The method of Claim 9 wherein said well-defined [zone] free volume has a transverse thickness which is essentially equal to a focal operating range of the [microscopical] microscope-like instrument at a predetermined power.

13.(amended) A method for detecting the presence or absence of circulating [target pathologically abnormal] hematopoietic progenitor nucleated cells in an anticoagulated whole blood sample, said method comprising the steps of:

a) providing [a] an at least partially transparent [tube] container having a bore which contains an [axially elongated] insert, said [tube] container and insert combining to form a well-defined [zone] free volume between said insert and a wall of said container bore [in the tube] which well-defined [zone] free volume has a transverse thickness that is at least about ten microns;

b) combining the blood sample with one or more [epitope-specific] labeling agents which are specific to surface receptors on hematopoietic progenitor cells so as to differentiate any [pathologically abnormal target nucleated] hematopoietic progenitor cells from other formed components in the blood sample;

c) combining the blood sample with a colorant which is operable to clarify [cell] cellular morphology in all nucleated cells in the blood sample;

d) placing the blood sample in the [tube] container and centrifuging the blood sample in the [tube] container so as to cause any [abnormal nucleated] hematopoietic progenitor cells present in the blood sample to gather in said well-defined [zone] free volume in the [tube] container;

e) examining the well-defined [zone] free volume under magnification and enumerating any differentiated hematopoietic progenitor cells found in situ in the well-defined [zone] free volume in the [tube] container;

f) examining under magnification the [cell] morphology of any differentiated cells in situ in the well-defined [zone] free volume in the [tube] container;

g) said combining steps being performed either before or after the blood sample is placed in the [tube] container; and

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h) said enumerating and examining steps being performed in no particular order.

14.(amended) A method for detecting the presence or absence of circulating [target nucleated] cancer cells in a centrifuged sample of anticoagulated whole blood contained in a [tube] container which [tube] container also contains [a generally cylindrical] an insert that forms a well-defined [annular zone] free volume in the [tube] container, said blood sample having been combined with one or more epitope-specific labeling agents that are operative to produce a characteristic signal result on [target nucleated] cancer cells, which result can include no signal at all, and which result is defined by the presence or absence of one or more epitopes on the [target nucleated] cancer cells, and said blood sample having also been combined with a colorant which is operable to clarify [cell] cellular morphology in all nucleated cells in the blood sample, said method comprising the steps of identifying by [cell] morphology all nucleated cells [that may be target cells and which are] disposed in said well-defined annular [zone] free volume, and further characterizing all identified nucleated cells as [target] cancer cells or [non-target] non-cancer cells epitopically, said identifying and characterizing steps being performed in situ in the [tube] container.

REMARKS

This is responsive to the grounds for rejection presented by Examiner Eyler in the final rejection put forth in the parent application office action dated March 13, 2000.

To begin with, there are a great number of §112 rejections put forth. These rejections will be addressed individually hereinafter.

THE §112 REJECTIONS

Claims 1, 2 and 8-13 have been rejected under 35 USC §112, (2nd para) as being vague and indefinite due the allegation that the phrase "pathologically abnormal" is not clearly defined in the specification. The Examiner alleges that there is no bright line between cell normality and cell abnormality. Applicants have pointed to the specification for guidance as to the meaning of the aforesaid phrase, and the Examiner has cited In re Van Geuns, 26 USPQ2d 1057 (Fed. Cir. 1993) for the proposition that limitations from the specification are not to be read into the claims